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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/245,603	02/05/1999	DAVID T. CURIEL	D6080	5072

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EXAMINER	
PARAS JR, PETER	
ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 02/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/245,603	CURIEL ET AL.	
	Examiner	Art Unit	
	Peter Paras, Jr.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,9,11,12,16,22 and 23* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,9,11,12,16,22 and 23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Applicant's amendment received on 4/23/02 has been entered. Claims 6-8 and 18-20 have been cancelled. Claims 1 and 16 have been amended. Claims 1-4, 9, 11-12, 16, and 22-23 are pending and are under current consideration.

Drawings

The formal drawings filed on 11/27/02 are accepted by the Examiner.

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The previous enablement rejection of claims 1-4, 6-7, 16, 18-20, and 22 under 35 U.S.C. 112, first paragraph, is withdrawn in light of the claim amendments.

Claims 9, 11-12 and 23 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The rejection of claims 9, 11-12, and 23 is maintained for the reasons advanced on pages 5-6 of the Office action mailed on 11/23/01.

Applicant's arguments filed on 4/23/02 have been fully considered but are not persuasive. Applicants continue to submit that a method of administering adenovirus that carries a herpes simplex virus-thymidine kinase gene to an individual followed by glanciclovir treatment is a standard treatment procedure used in a number of gene therapy trials. Therefore Applicants are of the opinion that it does not require undue experimentation for one skilled in the art to practice the claimed invention. See pages 5-6 of the amendment.

In response, the Examiner maintains that the art of gene therapy was unpredictable at the time the claimed invention was filed and has remained so thereafter. See Verma, Eck, and Sandhu as referenced in the Office action mailed on 11/23/01, and pages 4-5 of the Office action mailed on 2/28/01. It is further maintained the evidence of record has not provided guidance that correlates enhanced cellular uptake of the claimed adenoviral vector with killing of tumor cells *in vivo*.

Accordingly, the rejection is maintained for the reasons of record.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-4, 9, 11-12, 16, and 22-23 as originally filed or amended are rejected under 35 U.S.C. 102(e) as being anticipated by Wickham et al. The previous rejection is maintained for the reasons of record advanced in the Office action mailed on 11/23/01 on pages 6-7.

Applicant's arguments filed 4/23/02 have been fully considered but they are not persuasive. Applicants continue to argue that Wickham et al does not teach gene transfer to primary tumor cells using the adenoviral vector embraced by the claims. Applicants have argued that Wickham et al has not disclosed functional data for an adenoviral vector comprising an RGD insertion in the HI loop of the fiber protein. In light of such Applicants assert that the disclosure of Wickham et al does not enable an adenovirus with an RGD peptide inserted into the HI loop of the fiber protein. See pages 6-9 of the amendment.

In response, the Examiner maintains that Wickham et al anticipates the claimed invention for the following reasons: 1) Wickham et al has taught modification in the HI loop (see column 8); 2) the modification can be the insertion of a nucleic acid sequence encoding an RGD peptide (see columns 9 and 27); 3) Wickham et al has taught an

adenoviral vector comprising a nucleic acid sequence encoding HSV-TK (see column 14); 4) Wickham has taught gene transfer in tumor cells (see column 17); and 5) Wickham et al discusses that an adenovirus with a chimeric fiber protein, which comprises a non-native amino acid sequence, is able to direct entry into cells more efficiently (see column 6). See page 7 of the Office action mailed on 11/23/01. The Examiner asserts that Wickham et al has taught gene transfer into tumors *in vivo* (see column 17, at lines 1-10 and lines 36-45). If the tumor is *in vivo* then it is clearly a primary tumor cell. Moreover, in response to Applicant's argument that the disclosure of Wickham is not enabling for an adenovirus with an RGD peptide inserted into the HI loop of the fiber protein, it is understood that every patent is presumed valid (35 U.S.C. 282), and that presumption includes the presumption of operability (Metropolitan Eng. Co. v. Coe, 78 F.2d 199, 25 USPQ 216 (D.C.Cir. 1935). Also see MPEP 716.07. Further, since in a patent it is presumed that a process if used by one skilled in the art will produce the product or result described therein, such presumption is not overcome by a mere showing that it is possible to operate within the disclosure without obtaining the alleged product. In re Weber, 405 F.2d 1403, 160 USPQ 549 (CCPA 1969). It is to be presumed also that skilled workers would as a matter of course, if they do not immediately obtain desired results, make certain experiments and adaptations, within the skill of the competent worker. The failures of experimenters who have no interest in succeeding should not be accorded great weight. In re Michalek, 162 F.2d 229, 74 USPQ 107 (CCPA 1947); In re Reid, 179 F.2d 998, 84 USPQ 478 (CCPA 1950).

Accordingly, the rejection is maintained for the reasons of record.

The following are new grounds of rejection under 35 USC § 103:

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 16 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wickham et al.

The claims are directed to a method of increasing the ability of an adenovirus to transduce primary tumor cells, wherein the tumor cell is a cancer ascite sample or a primary explant.

Wickham et al has taught modification in the HI loop (see column 8), wherein the modification can be the insertion of a nucleic acid sequence encoding an RGD peptide (see columns 9 and 27). Wickham has taught gene transfer in tumor cells (see column 17). In particular, Wickham et al has taught gene transfer into tumors *in vivo* (see column 17, at lines 1-10 and lines 36-45). If the tumor is *in vivo* then it is clearly a primary tumor cell. Wickham et al discusses that an adenovirus with a chimeric fiber protein, which comprises a non-native amino acid sequence, is able to direct entry into cells more efficiently (see column 6).

Wickham et al does not teach a method of transducing primary tumor cells, wherein the tumor cell is a cancer ascite sample of a primary tumor explant.

At the time the claimed invention was made, *in vitro* transduction of primary tumor explants was within the routine skill level of the ordinary artisan. In particular, *in vitro* transduction of primary tumor cell explants was routine practice for testing the gene delivery efficiency of a particular vector prior to *in vivo* use.

Accordingly, in view of the routine state of the art, it would have been obvious to modify the method of Wickham by using tumor cells that are tumor cell explants with a reasonable expectation of success. One of ordinary skill in the art would have been sufficiently motivated to make such a modification as it was an art-recognized goal to test the gene delivery efficiency of a vector *in vitro* prior to *in vivo* use.

Thus, the claimed invention, as a whole, was clearly *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Peter Paras, Jr., whose telephone number is 703-308-8340. The examiner can normally be reached Monday-Friday from 8:30 to 4:30 (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at 703-305-4051. Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703) 308-4242 and (703) 305-3014.

Inquiries of a general nature or relating to the status of the application should be directed to Dianiece Jacobs whose telephone number is (703) 305-3388.

Peter Paras, Jr.

Art Unit 1632

PETER PARAS
PATENT EXAMINER